IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Group Art Unit 1614

In re

Patent Application of

Yung-Hi Kim, et al.

Serial No.: 10/509,300

Filed: 9/24/2004

Confirmation No.: 3662

Examiner: Michel Graffeo

"NOVEL THERAPEUTICAL USE OF AGONIST LIGANDS SPECIFIC TO G2A RECEPTOR"

I, Tracy Bruesewitz, hereby certify that this correspondence is being electronically filed with the U.S. Patent and Trademark Office on the date of my signature.

Signature

September 22, 2006

Date of Signature

DECLARATION UNDER 37 CFR 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Dong-Keun Song, M.D., Ph.D., hereby declare and state the following:

1. I currently hold the position of Professor, Department of Pharmacology at the College of Medicine at Hallym University in the Republic of Korea.

2. I received the degree of Medical Doctor in 1981 at the College of Medicine at Seoul National University. I earned an M.S. degree in 1986 and a Ph.D. degree in 1989, both in Pharmacology, at the College of Medicine at Seoul National University. I completed a Post-Doctoral Fellowship in the Neuronal Development Program at Colorado State University in 1990. My curriculum vitae is attached as Exhibit A.

3. I consider myself an expert in pharmacology. I have published over 50 articles in peer-reviewed journals on topics pertaining to this subject.

4. I make this declaration in support of the prosecution of U.S. Patent Application Serial No. 10/509,300 before the United States Patent and Trademark Office. I am a joint inventor of the subject matter of all pending claims in the above-noted application.

5. In general, the present invention relates to methods effective for treating or preventing diseases or disorders associated with suppression of neutrophil apoptosis or excessive release of IL-8. The methods comprise administering a lysophosphatidylcholine ("LPC") compound of formula I (formula omitted), a sphingosylphosphorylcholine ("SPC") compound of formula II (formula omitted) or an ether derivative of LPC (formula omitted). As stated in the specification, the methods of the claimed invention can be used in the treatment or prevention of diseases or disorders associated with neutrophil accumulation due to suppression of apoptosis and neutrophil hyperactivity and/or excessive release of IL-8, especially inflammatory diseases, such as ischemia reperfusion injury and sepsis. (See, e.g., specification at page 14).

6. It is my understanding that the Examiner has rejected claims 6-18, 21-22 and 24-29 on the basis that although the specification is enabling "for a method of inhibiting IL-8 in vitro and treating sepsis to the extent that survival rates of septicemia induced mice are better as compared to the control," the specification allegedly "does not reasonably provide enablement for the treatment and/or prevention of any and all diseases associated with IL-8, i.e. Gerhardt disease and ischemia-reperfusion injury." More specifically, the Examiner has asserted that "no working examples are provided for <u>preventing</u> [ ] any and all diseases associated with IL-8" and the "Applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the <u>preventative</u> effects of the instant composition." (See Office Action at pages 4-6, emphasis added).

7. In response to the Examiner's concerns regarding the ability of the claimed compositions to prevent IL-8-associated diseases or disorders, I performed the following experiment to demonstrate the preventative effects of 1-stearoyl LPC in a well-established mouse model of sepsis. Fifteen BALB/c mice (each weighing about 25-30 g) were divided into three groups of five. Each group of five was injected subcutaneously with either 10 mg/kg of 1-stearoyl LPC, 20 mg/kg of 1-stearoyl LPC or fatty-acid free 1% bovine serum albumin (BSA) solution (control) fifteen minutes before injecting $5x10^8$ bacteria into the abdominal cavity of the mice. After 8 hours, the number of peritoneal bacteria remaining was estimated.

8. As shown in Exhibit B attached hereto, the number of bacteria cleared by BALB/c mice, in colony forming units (CFU ($x10^5$)) per unit volume of peritoneal fluid, after pre-treatment with 1-stearoyl LPC (10 mg/kg or 20 mg/kg) was significant in comparison to that of the control (BSA) group. Thus, 1-stearoyl LPC was effective in preventing sepsis in a well-established animal model.

9. I submit that the results of this experiment provide evidence supporting the statements in the specification that the claimed compositions have the ability to prevent sepsis. Based on the evidence provided herein and in the specification, a worker in the field would expect that these results could be extrapolated to the other diseases or disorders recited in the claims, based on their common etiologies, i.e., suppression of neutrophil apoptosis and/or excessive release of IL-8.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: Aug. 23th 2006 DONG-KEUN SONG DongKeun Song

Docket No.: 013709-9001-US00
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CURRICULUM VITAE

EXHIBIT A

NAME: Dong-Keun Song, M.D., Ph.D.

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ACADEMIC EDUCATION:

1981	M.D. College of Medicine, Seoul National University, Seoul, Korea
1986	M.S. Pharmacology, Seoul National University, Seoul, Korea
1989	Ph.D. Pharmacology, Seoul National University, Seoul, Korea
1990	Post Doctoral Fellow, Program in Neuronal Development, Colorado State University, USA.

APPOINTMENTS AND PROFESSIONAL ACTIVITIES:

1984-1986	Teaching Assistant, College of Medicine, Seoul National University
1986-1988	Instructor, Department of Pharmacology, College of Medicine, Hallym University
1988-1990	Assistant Professor, Department of Pharmacology, College of Medicine, Hallym University
1993-1998	Associate Professor, Department of Pharmacology, College of Medicine, Hallym University
1998-present	Professor, Department of Pharmacology, College of Medicine, Hallym University
2005-present	Director of Infectious Disease Medical Research Center, Hallym University

RESEARCH FIELDS

1. Development of protective agents against sepsis and studies on their mechanisms of actions.

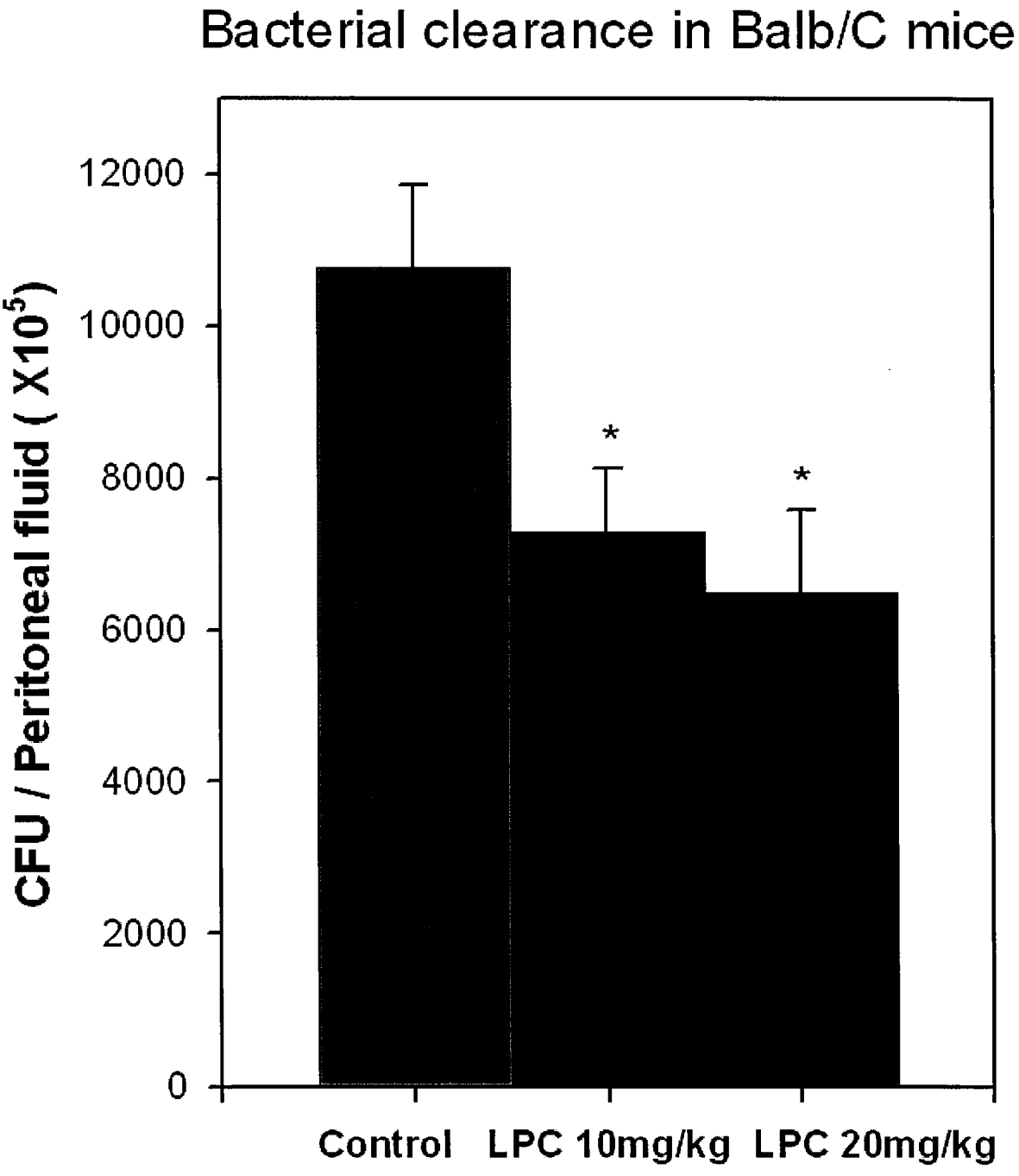
To develop protective agents against sepsis, we are currently examining the effects of various agents on animal models of sepsis and their mechanisms. Currently we are focusing on the effects of lysolipids.

2. Pharmacological evaluation of lysophosphatidylcholine.

REPRESENTATIVE PUBLICATIONS

1. Yan JJ, Jung JS, Lee JE, Lee J, Huh SO, Kim HS, Jung KC, Cho JY, Nam JS, Suh HW, Kim YH, Song DK. Therapeutic effects of lysophosphatidylcholine in experimental sepsis. Nat Med. 2004;10(2):161-7.
2. Yan JJ, Cho JY, Kim HS, Kim KL, Jung JS, Huh SO, Suh HW, Kim YH, Song DK. Protection against beta-amyloid peptide toxicity in vivo with long-term administration of ferulic acid. Br J Pharmacol. 2001;133(1):89-96.
3. Song DK, Im YB, Jung JS, Cho J, Suh HW, Kim YH. Central beta-amyloid peptide-induced peripheral interleukin-6 responses in mice. J Neurochem. 2001;76(5):1326-35.
4. Song DK, Im YB, Jung JS, Yan JJ, Huh SO, Suh HW, Kim YH. Central injection of nitric oxide synthase inhibitors increases peripheral interleukin-6 and serum amyloid A: involvement of adrenaline from adrenal medulla. Br J Pharmacol. 2000;130(1):41-8.
5. Song DK, Im YB, Jung JS, Suh HW, Huh SO, Song JH, Kim YH. Central injection of nicotine increases hepatic and splenic interleukin 6 (IL-6) mRNA expression and plasma IL-6 levels in mice: involvement of the peripheral sympathetic nervous system. FASEB J. 1999;13(10):1259-67.
6. Song DK, Im YB, Jung JS, Suh HW, Huh SO, Park SW, Wie MB, Kim YH. Differential involvement of central and peripheral norepinephrine in the central lipopolysaccharide-induced interleukin-6 responses in mice. J Neurochem. 1999;72(4):1625-33.

EXHIBIT B


Bacterial clearance in Balb/C mice
CFU / Peritoneal fluid (X10^5)
12000
10000
8000
6000
4000
2000
0
*
*
Control
LPC 10mg/kg
LPC 20mg/kg